PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING TRANSMITTAL OF COPY OF INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (CHAPTER I OF THE PATENT COOPERATION TREATY)
(PCT Rule 44bis.1(c))

To:

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Date of mailing *(day/month/year)* 03 August 2006 (03.08.2006)	
Applicant's or agent's file reference 10003121WO01	IMPORTANT NOTICE
International application No. PCT/JP2005/000811	International filing date *(day/month/year)* 18 January 2005 (18.01.2005)
Priority date *(day/month/year)* 23 January 2004 (23.01.2004)	
Applicant CANON KABUSHIKI KAISHA et al	

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)

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PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference 10003121WO01	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/JP2005/000811	International filing date *(day/month/year)* 18 January 2005 (18.01.2005)	Priority date *(day/month/year)* 23 January 2004 (23.01.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant CANON KABUSHIKI KAISHA		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 24 July 2006 (24.07.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Yoshiko Kuwahara
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Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

REC'D 27 JUL 2005
WIPO PCT

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

4/8

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

	Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2005/000811	18.01.2005	23.01.2004

International Patent Classification (IPC) or both national classification and IPC
G01N33/543, G01N33/52

Applicant
CANON KABUSHIKI KAISHA

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Authorized Officer
European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Sitch, W Telephone No. +31 70 340-3040

Form (PCT/ISA/237) (Cover Sheet) (January 2004)

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material:

      ☐ in written format

      ☐ in computer readable form

   c. time of filing/furnishing:

      ☐ contained in the international application as filed.

      ☐ filed together with the international application in computer readable form.

      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	7-11
	No:	Claims	1-6
Inventive step (IS)	Yes:	Claims	None
	No:	Claims	1-11
Industrial applicability (IA)	Yes:	Claims	1-11
	No:	Claims	None

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:
D1: WO0107653
D2: WO9917119
D3: Lab on a Chip, 2001, 1, 153-157
D4: Analytical Sciences, 19, 2003, 15-22
D5: Pure Appl. Chem., 74, 2002, 2299-2309
D6: Anal. Chem.,74, 2002, 379-385
D7: Anal. Chem.,75, 2003, 1116-1122

Attention is drawn in particular to all passages of these documents as indicated on the International Search Report, unless stated otherwise.

1. Subject matter of the application

The present application is predicated on the use of the known laminal flow technique for the detection of substances in a fluid sample under analysis. In the phenomenon of laminal flow of liquids, the dimensions of channels located in a device (here, the 'detecting element' of claim 1 of the present application) are chosen such that when a fluid sample is applied to such a channel, the liquid under analysis will flow therein as a plurality of 'layers' ('lamina'). In the present application, in exploiting the fact that the fluid sample applied to such channel ('microchannel') may be considered to flow as a plurality of essentially independent fluid layers, a plurality of 'detecting means' (the 'substance trapping portions' of claim 1) are located in the channel in such a way that a plurality of substances in the fluid sample may be analysed / detected within a single (microfluidics) device.

Claim 1:

A detecting element, having a) a channel able to form a plurality of layers of flow of a liquid [ie of appropriate dimensions such that liquids applied thereto flow in a laminar fashion - eg page 12 of application, dimensions of 100μm width and 100μm depth], b) a plurality of 'substance trapping portions' in the channel, c) said elements b) being separated and

arranged to independently acquire information on each of the substances in the sample being analysed.
Fig. 2 of the application shows how such elements of a microfluidic device may be envisaged, especially with respect to the relation between the microchannel and detecting elements.

Claim 7:
Effectively the means of the present application for using the device recited in claim 1.

Other claims:
Specification of various preferred embodiments of the device / the use thereof, eg with respect to the substance trapping portions of the device, such have antibody immobilised thereon [the antibody for example binding to an analyte present in the fluid sample under analysis].

2. Prior Art.
D1: Microchannel based device / means for detecting different analytes in a sample after their binding to their cognate binding partners. Such binding partners are immobilised in different sections of the microchannel. In use, sample is passed down the microchannel, target analyte retained, the remainder of sample eluted; thereafter, bound analyte is released and detected / measured. The microchannel preferably has two or more immobilised binding partners specific for two or more analytes to be analysed, located in different regions of the microchannel; upon release of two or more analytes from two or more binding partners, segregation of analytes remains, and the analytes can be separately detected. See D1, page 2, line 20 -page 4, line 21.
D2: Microfluidic devices in detection of analytes. Makes reference to various techniques which can be used in detection means (eg fluorescence, chemiluminescence).
D3: ELISA on a microchip
Other prior art, D4-D6: Microfluidic systems, see comments hereinafter; **D7**: protein chip with antibodies for detection, see comments hereinafter.

3. Novelty (Art. 33(2) PCT)

- In light of D1, the subject matter of claims 1, 2, 6 (D1, page 2, lines 23, 24, binding partner for binding analytes can be an antibody) clearly lacks novelty.

- At present the subject matter of claim 7 is unclear, since the nature of the technical feature apparently sought to be specified by the phrase beginning 'switching and passing ...' is unclear. In order to be able to give an opinion on novelty and inventive step of the subject matter of this claim, interpretation has been made that this phrase reads 'thereafter passing though the channel in which the plurality of different substances have been trapped a fluid which enables the acquisition of independent information on each of the substances in the specimen through an action between the fluid and the trapped substance'. In D1, analytes in a sample which have been previously bound (trapped) in the microchannel are released and flushed past a detector (D1, page 2, lines 29, 30), the spatial segregation of the released analytes being maintained (D1, page 3, lines 10-12). Over D1, the subject matter of claim 7, and claims 8-11 dependent thereon, thus appears to be novel.

- Claims 3-5 specify (recite) technical features of the specimen (sample) to be used in (ie passed through) the detecting element of claim 1, and as such do not specify any further technical features of the device being claimed in claim 1. Accordingly, the subject matter of these claims also lacks novelty in light of D1.

4. Inventive Step (Art. 33(3) PCT)

Whilst possibly novel, the subject matter of claim 7 lacks inventive step for the following reasons. The acquisition of information on a substance trapped or otherwise present in a microfluidic channel by passing a fluid over or in the neighbourhood of the substance, and wherein the fluid comprises an element interacting with the substance to produce a detectable signal indicative of the presence of the substance would appear routine in the art. As an example of this technique, see for example D2, page 2, line 2 - page 3, line 6; examples on pages 19, 20, figures 1 and 10, and D3, page 154, paragraphs 1-3, figure 1. Accordingly, the subject matter of claim 7, and in addition that of claims 8-11 lacks inventive step (the additional features recited in claims 8-11 also appearing to be features which would be derived as a matter of routine practise in the field concerned).

5. Other comments

There would appear no other subject matter in the application as filed which is both novel and inventive. In this respect, the following comments should be noted.

5.1 Use of each of the enzymes listed in claim 5 in the detection of entities in assays (eg immunoassays) is routine in the art. See eg D6, page 384, figure 7; D7, page 1116, paragraph 2 - page 1119, paragraph 1. The latter document also details antibody based detection methods for human AFP and human β2-microglobulin using antibodies to these entities as 'capture antibodies (D7, page 1117, bottom of left hand column); the examples of the present application are concerned with the capture and detection of exactly the same entities.

5.2 Concerning the preferred microchannel devices of the present application as schematically drawn in figures 1/3 and 7:

these devices have a microchannel arrangement ('principle microchannel') such as of the nature disclosed in D1 and as discussed hereinabove, 'substance trapping portions' arranged in said microchannel as per D1, and the additional features as compared to D1 of having two (fig. 1/3) or three (fig. 7) microchannel branches 'preceding' the 'principle microchannel'. Such arrangement of microchannels whilst apparently novel over D1 is broadly known from other items of prior art: see for example D4, page 17, figure 4; D5, page 2302, figure 3, page 2303, figure 5, page 2306, figure 8; D6, page 383, figure 5.